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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,275	02/11/2005	Benjamin Geiger	29140	9948

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EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,275	GEIGER, BENJAMIN	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *July 23, 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22 and 42-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22 and 42-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office Action is in response to the paper filed July 23, 2007. Applicant's election without traverse of Group VI, claims 16-22 and new Claim 42 in the reply filed on December 12, 2006 is acknowledged.

Claims 1-15 and 23-41 have been cancelled. Claims16-22 and 42-61 are currently under examination.

Benefit of priority is granted to August 20, 20002.

Maintenance of Rejections:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-22 and 42-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 16, it is not clear how one will "provide" a chimeric polypeptide to an organism or "expose" an organism to a detectable molecule. Also, the addition of "or virus" is not art recognized, that is, a virus is DNA and does not comprise a cell compartment, for example. See also Claim 43, 46, 54. The method of Claim 16 is also indefinite because the method is to "highlight", and to determine the presence or absence of a cell compartment, biological component, or macromolecule. If the cell compartment, biological component, or macromolecule is not present then it cannot be highlighted. See also Claims 44, 52.

In Claim 18, there is no antecedent basis for expressing the chimeric polypeptide in an organism in Claim 16. As noted in the previous office action, to express the chimer would be to

provide a nucleic acid encoding the chimer, not the chimer itself. Additionally, a virus does not express the heterologous DNA. See also Claims 47, 55.

It appears that Applicants should reconsider their claims because a virus is a DNA that does not comprise a cell compartment and its biological component and macromolecule is DNA. Viruses do not replicate/express DNA. Rather, infected cells replicate and express the viral DNA.

Applicants state that the chimeric polypeptide can be administered to or expressed in an organism. These methods are wholly different and is the point of this aspect of the rejection. As noted in the rejection, to express the chimer would be to provide a nucleic acid encoding the chimer, not the chimer itself.

Applicants state that they have amended Claim 18 to state that they are providing the nucleic acid encoding the chimer to the organism or virus. As noted in the rejection, Claim 16 is limited to providing the chimer itself, not the nucleic acid.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-22 and 42-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the BRET method for determining macromolecule identification in E. coli as set forth by Xu et al. below, does not reasonably provide enablement for method of highlighting a cell compartment, biological component, or other macromolecules that are endogenous to the organism, or in a multicellular organism or virus. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed invention is drawn to a method for highlighting a cell compartment or biological component, or macromolecule in an organism by providing a chimeric polypeptide to the organism. The chimer will comprise a portion that specifically binds to a detectable molecule and comprise a portion that will specifically bind to biological component, bind to a macromolecule, or target a specific cell compartment. After the organism has the chimer situated therein, the organism is to be exposed to the detectable molecule, which will be bound by the chimer, and the detectable molecule detected (indirectly) bound to the biological component or macromolecule, or detected in a specific cell compartment. The invention is set forth prophetically in the specification.

In *In re Wands* (858 F2d, 731, 737, 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the issue of enablement in molecular biology was considered. It was held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation:

1) Quantity of experimentation necessary: One skilled in the art would have to devise their own experiments to determine how to highlight a cell compartment, biological component, or macromolecule endogenous to an organism.

2) Amount of direction or guidance presented: The specification does not state why one of ordinary skill in the art would want to target a cell compartment or biological component, or macromolecule in an organism. The specification does not teach how one would choose a detectable molecule, and make a polypeptide that can bind to this detectable molecule in the form of a chimeric polypeptide with the targeting polypeptide. The detectable molecule must be administered to the organism and bind to the chimer. It is not taught how this detectable molecule will be "packaged" to be able to traverse cell membranes and cellular compartments

to bind to a chimer targeted to cell compartments are intracellular components and macromolecules. If the detectable molecule does finds its way to the chimer, the specification does not teach how one skilled in the art would detect it in an organism.

3) Presence or absence of working examples: There are no working examples. The examples provided are prophetic.

4) Nature of the invention; 5) State of the prior art; 6) Relative skill of those in the art: The nature of the art is complex and the state of the prior art does not recognize targeting proteins that bind to a detectable molecule to cell compartments, biological components, or macromolecules in multicellular organisms.

7) Predictability or unpredictability of the art: Because such methods are not known, the art is not predictable.

8) Breadth of the claims: The claims are broad.

For all of these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

Applicants argue Factors 1 and 2 without consideration for what is not enabled. The non-enabled aspects of the inventions are drawn to cell compartment, biological component, or other macromolecules that are endogenous to the organism, or in a multicellular organism or virus.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16-22, 44, 45, 47-53, 55-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. (1998; A bioluminescence resonance energy transfer (BRET) system: Application to interacting circadian clock proteins. Proc Natl Acad Sci U S A. 1999 January 5; 96(1): 151–156).

At page 154, right col. para. 2, Xu et al. teach teach making fusion constructs of clock protein kaiB to EYFP and Rluc and transforming E. coli with these constructs. Xu et al. added coelenterazine (see page 152, right col., para. 2, penultimate sentence) to the E. coli culture to and measured bioluminescence emission spectra via a spectrofluorometer with a xenon lamp (see page 152, right col., para. 2, line 10-11) as an indication of the formation of KaiB homodimers within the E. coli.

Therefore, Xu et al. teach a method of highlighting a macromolecule (KaiB) in an organism by providing a chimeric polypeptide comprising KaiB:Rluc and KaiB:EYFP and exposing the organism to a detectable molecule coelanterazine (**Claim 16, 44, 52**), wherein the organism is a bacterium E. coli (**Claim 17, 45, 53**), where in the chimer is expressed within the organism (**Claim 18, 47, 55**), wherein the detectable molecule coelanterazine is administered to the organism (**Claim 19, 48, 56**), wherein the detectable molecule was visualized (**Claim 20, 49, 57**) with a microscope (**Claim 21, 50, 58**) equipped with a light source (**Claim 22, 51, 59**). **Claim 60 and 61** are included in this rejection because clock proteins are cell specific and the protein was localized in the E. col.

Applicants urge that highlighting a macromolecule in E. Coli is not the point of Xu et al. The motivation of Xu et al. is not germane to the rejection. Xu et al. performed the instant invention, and therefore the teachings of Xu et al. is prior art against the claims.

Applicants urge that Xu et al. do not teach the absence or presence of a cell compartment, biological component, or macromolecule. The observation of the presence of KaiB fulfills this step.

Applicants urge that Claim 60 reads over Xu etal. because the KaiB is not cell specific and is foreign to the cell. The claims are drawn to organisms and to viruses, not to cells. Regarding Claim 61, the KaiB was located and, therefore, localized.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER